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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,169	11/28/2005	Roger R. C. New	117-565	7760

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EXAMINER	
BRADLEY, CHRISTINA	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 05/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/553,169	NEW, ROGER R. C.	
	Examiner	Art Unit	
	Christina Bradley	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/17/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Status of Claims

1. Claims 1-25 are pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 16-23 provides for the use of a non-conjugated bile acid or salt and either propyl gallate or BHA, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 16-23 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 6-10, 12, 13, 15-20 and 23-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Soltero *et al.* (US 20030069170). Soltero *et al.* teach a pharmaceutical composition comprising an active macromolecular principle such as a polypeptide (see paragraph 0038), a non-conjugate bile salt (see abstract) and an additive such as a derivative of propyl gallate (see paragraph 0228, propyl benzoates include propyl 3,4,5-trihydroxybenzoate which is another name for propyl gallate, see registry file for RN 121-79-9). Soltero *et al.* teach that the pharmaceutical composition described above can be a solution (see claim 13) or a solid (see claim 15). Soltero *et al.* teach that the pharmaceutical composition described above can comprise insulin (see paragraph 0083), calcitonin (see paragraph 0057), growth hormone (see paragraph 0079), or parathyroid hormone (see paragraph 0103) or derivatives thereof. Soltero *et al.* teach that the bile salt can be chenodeoxycholate (see paragraph 0147). Soltero *et al.* teach methods of administering the pharmaceutical composition described above and using the pharmaceutical composition to treat diseases (see paragraph 0015).

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soltero *et al.* (US 20030069170). Soltero *et al.* teach a pharmaceutical composition comprising an active macromolecular principle such as a polypeptide (see paragraph 0038), a non-conjugate bile salt (see abstract) and an additive such as a derivative of propyl gallate (see paragraph 0228, propyl benzoates include propyl 3,4,5-trihydroxybenzoate which is another name for propyl gallate, see registry file for RN 121-79-9), as described above. Soltero *et al.* do not teach the specific proportions of ingredients recited in claims 4 and 5. It would have been obvious to one of ordinary skill in the art to optimize the concentration of macromolecular principle, bile salt and additive to maximize effectiveness. One would have been motivated to do so because Soltero *et al.* teach that the amount of each of these ingredients can affect the performance of the pharmaceutical composition.

10. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical (see MPEP 2144.05). "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable

ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977). In the present case, the concentration of the macromolecular principle in the pharmaceutical composition is critical and must be optimized to effectively treat a specific disease. Soltero *et al.* teach that the amount of bile salt affects the behavior of other components of the composition and therefore must also be optimized. Finally, Soltero *et al.* teach that the derivative of propyl gallate can be included as preservative. The amount of preservative added is critical and would depend on the size of the pharmaceutical composition, the concentration of active ingredients and the storage conditions intended for the product as well as other factors. There would have been a reasonable expectation that the concentration of the ingredients could be successfully optimized given that such experimentation is routine. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

11. Claims 13 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soltero *et al.* (US 20030069170) as applied to claims 1, 4 and 5 above in further view of Lacy & Embleton (USPN 5,645,856). Soltero *et al.* teach that preservatives can be added to the pharmaceutical composition in addition to a macromolecular principle and a bile salt (see paragraph 0228). Soltero *et al.* do not specifically teach the addition

of butyl hydroxyanisole (BHA) as an additive in the pharmaceutical composition described above. Lacy & Embleton teach the delivery of hydrophobic drugs in a composition comprising a bile salt (see column 18, line 61) and additional additives such as butyl hydroxyanisole or propyl gallate (see column 13, line 63).

12. It would have been obvious to one of ordinary skill in the art to combine the macromolecular drug and bile salt taught by Soltero *et al.* and propyl gallate or butyl hydroxyanisole taught by Lacy & Embleton. The skilled artisan would have been motivated to do so given that Lacy & Embleton teach that butyl hydroxyanisole and propyl gallate may be added to pharmaceutical compositions designed to enhance the solubility of drugs. There would have been a reasonable expectation of success given that butyl hydroxyanisole and propyl gallate are considered to be common additives. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

13. Claims 11 and 21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soltero *et al.* (US 20030069170) as applied to claims 1, 4 and 5 above in further view of Bradley (*Int. Crit. Care Nursing*, **2002**, *18*, 189-191). Soltero *et al.* teach that the active macromolecular principle can be insulin (see paragraph 0083). Soltero *et al.* do not teach the addition of an insulin sensitizing agent. Bradley teaches the glitazone family, a class of insulin-sensitizing drugs (see page 189, column 2).

14. It would have been obvious to one of ordinary skill in the art to combine the insulin, bile salt and propyl benzoate taught by Soltero *et al.* and a glitazone as taught

by Bradley. The skilled artisan would have been motivated to do so given that glitazones enhance insulin in adipose tissue and skeletal muscle and reduce insulin resistance. There would have been a reasonable expectation of success given that Bradley teaches that members of the glitazone family are licensed for use as a diabetes treatment. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

15. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Soltero *et al.* (US 20030069170) as applied to claims 1, 4 and 5 above in further view of New (USPN 5,853,748) and Russell-Jones (WO0022909). Soltero *et al.* teach a pharmaceutical composition comprising a polypeptide such as insulin and a bile salt in the form of a solid. Soltero *et al.* do not teach an enteric coating for the pharmaceutical composition. New teaches an enteric coating for the oral administration of insulin and a bile salt (see column 1, lines 40-45). Russell-Jones describes enteric coatings of insulin (see abstract).

16. It would have been obvious to one of ordinary skill in the art to combine the insulin, bile salt and propyl benzoate taught by Soltero *et al.*, and use it in tablet form with an enteric coating which becomes permeable at pH 3 to 7 as taught by New and Russel-Jones. One would have been motivated to do so because New and Russell-Jones suggest that such an enteric coating will prevent the degradation of insulin in the stomach, allowing for its digestion in the small intestine. There would have been a reasonable expectation of success given that New and Russell-Jones teach such

enteric coatings for the oral administration of insulin. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

17. Claims 2 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Soltero *et al.* (US 20030069170) as applied to claims 1, 4 and 5 above in further view of Strickley & Anderson (*J. Pharm. Sci.*, **1997**, *86*, 645-653) and Harsch *et al.* (*Med. Sci. Monit.*, **2001**, *7*, 833-836). Soltero *et al.* teach a pharmaceutical composition comprising a polypeptide such as insulin and a bile salt in the form of a solid. Soltero *et al.* do not teach the specific proportion of water recited in claims 2 and 22. Strickley & Anderson teach the effect of water on the degradation of solid insulin (see abstract and introduction). Harsch *et al.* teach that active insulin is available in a solid powder (see abstract).

18. It would be obvious to one of ordinary skill in the art to optimize the water concentration of the pharmaceutical composition. One would be motivated to do so given that Strickley & Anderson teach that water can lead to degradation of insulin in the solid form. Generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration is critical (see MPEP 2144.05). In the present case, Strickely & Anderson teach that the level of hydration in the solid form is critical for storage and long-term activity of the pharmaceutical composition. There would have been a reasonable expectation that the water concentration could be successfully optimized given that

active insulin is available in a solid powder form as taught by Harsch *et al*. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

19. No claims are allowed.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Bradley whose telephone number is (571) 272-9044. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

21. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

22. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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